

1033-115 Impact of Diabetes Mellitus on Abnormal Heart Rate Recovery After Exercise

Andrea De Lorenzo, Adriana J. Soares, Ronaldo L. Lima, Estacio de Sa University, Rio de Janeiro, Brazil, Federal University of Rio de Janeiro, Brazil

Background: Abnormal heart rate recovery (HRR) after exercise has been the subject of extensive investigations due to its association with increased mortality. Its pathophysiology has been linked to autonomic imbalance but is still a matter of debate. This study aimed to determine the relationship between diabetes mellitus, a condition with a known high prevalence of autonomic neuropathy, and abnormal HRR after exercise. **Methods:** 2,189 consecutive patients (59% males, age 56.7 ± 10.5 years) who underwent exercise/rest Tc-99m sestamibi myocardial perfusion single-photon emission computed tomography (SPECT) were studied. Patients taking beta-blockers or calcium-channel antagonists were excluded. A symptom-limited exercise treadmill test (ETT) was performed according to a Bruce protocol. Myocardial perfusion SPECT was semiquantitatively analyzed using a 17-segment left ventricular model and a 5-point scale (graded from 0-normal tracer activity, to 4-absence of detectable tracer activity). Summed stress and rest scores (SSS, SRS) were obtained by adding segmental scores from stress and rest images, respectively; the summed difference score (SDS) was calculated as the difference between SSS and SRS. A multivariate analysis was used to determine the independent predictors of abnormal HRR among clinical, ETT and SPECT variables. **Results:** 253 patients (11.6%) were diabetics. Abnormal HRR at 1 minute after exercise was more prevalent among diabetics than nondiabetics (17.4% vs 12.4%; $p<0.05$). On multivariate analysis, however, after adjustment for other variables, diabetes was not an independent predictor of abnormal HRR. For the overall population, as well as for the subgroup of diabetic patients, the significant predictors of abnormal HRR were age ($p<0.0001$), resting heart rate ($p<0.0001$), inability to reach 85% of maximal predicted heart rate ($p<0.005$), exercise duration ($p<0.0001$), and the SRS ($p=0.01$). **Conclusion:** The mechanisms underlying abnormal HRR may be unrelated to diabetic autonomic neuropathy. Abnormal HRR is significantly related to perfusion defect extent and severity at rest and may most likely be a consequence of previous myocardial damage.

1033-116 Optimizing Exercise Protocols for Heart Failure Trials

Rochelle L. Goldsmith, Joshua W. Trufant, Gillian M. Mueller, M. Allison Arwady, Daniel Burkhoff, Columbia University, New York, NY

Background: Peak oxygen consumption (PVO_2) is often the primary endpoint in heart failure (CHF) trials. Ramped treadmill protocols 8-12 min in duration yield cleaner PVO_2 data and a more accurate estimate of exercise capacity. We sought to provide a framework for developing ramped protocols consistent with these guidelines that target CHF populations of various severities.

Methods: We conducted a retrospective study of 465 consecutive exercise tests of CHF pts with $\text{PVO}_2 \leq 20.0$ ml/kg/min. All tests were done on the Modified Naughton treadmill protocol (MNTP), the standard protocol for testing CHF pts. We excluded all sub-maximal tests ($\text{RER} \leq 1.09$) and stratified severity of CHF by defining ranges of PVO_2 . To quantify peak workload, we converted the speed and grade reached by each pt to METs using the American College of Sports Medicine algorithm (e.g., 2.0 mph, 7.0% grade=6.4 METs during min 10 and 11 of the MNTP).

Results: The table indicates the mean peak workload achieved by pts in each PVO_2 range.

Peak VO_2 (ml/kg/min)	Peak Workload (METs)
≤ 10.0	3.44 ± 1.28
$10.0 < \text{VO}_2 \leq 12.0$	4.24 ± 1.15
$12.0 < \text{VO}_2 \leq 14.0$	5.24 ± 1.19
$14.0 < \text{VO}_2 \leq 16.0$	5.92 ± 1.30
$16.0 < \text{VO}_2 \leq 18.0$	6.70 ± 1.25
$18.0 < \text{VO}_2 \leq 20.0$	7.26 ± 1.65

The MNTP tests performed by pts with $\text{PVO}_2 \leq 12$ ml/kg/min or >16 ml/kg/min were too short or too long, respectively, to fall in the range 5.4-6.4 METs demanded at min 8-12 of the MNTP.

Conclusion: Given the peak workload guidelines above, new ramped protocols can be tailored to a trial's target CHF functional class. For example, a ramped protocol that increases 1 mph and 1% grade each min would reach a workload range of 3.9-5.8 METs in min 8-12, which would be appropriate for patients with moderate to severe CHF.

1033-117 Ventilatory Response to Early Phase of Exercise: An Useful Index for Comprehensive Clinical Assessment of Patients With Heart Failure and Novel Predictor of Prognosis

Tomasz Witkowski, Ewa Jankowska, Robert Zymlinski, Agnieszka Kus-Klinowska, Waldemar Banasiak, Piotr Ponikowski, Military Hospital, Wroclaw, Poland

Background. Assessment of ventilatory response to exercise has been applied for the clinical evaluation and risk stratification in pts with chronic heart failure (CHF). In most studies ventilatory data were derived from the whole maximal cardiopulmonary exercise testing (CPX). Whether, ventilatory response to early phase of exercise carries comparable clinical and prognostic information remains unknown.

Methods. We investigated 202 consecutive CHF pts (175 men, age: 59 ± 11 yrs, NYHA class I/II/III/IV: 16/101/66/19; LVEF: $32 \pm 8\%$) who underwent CPX. Ventilatory response to exercise, expressed as VE-VCO2 slope was calculated 1) throughout the whole CPX (VE-VCO2 100%) and 2) throughout early phase of exercise - i.e. the first 180 seconds

(VE-VCO2 180s).

Results. CHF pts demonstrated decreased peak oxygen consumption (peakVO2, mean: 15.2 ml/kg/min) and elevated values of VE-VCO2 100% and VE-VCO2 180s (mean: 35.8 and 34.4 , respectively, all $p<0.0001$ vs reference values in our laboratory). Ventilatory response to early and whole exercise were strongly interrelated ($r=0.63$, $p<0.0001$). Augmented VE-VCO2 180s identified pts with more advanced disease by the relations with peakVO2: $r=-0.38$ ($p<0.0001$), quality of life assessed using Minnesota questionnaire score: $r=0.26$ ($p<0.05$), NYHA class: $r=0.23$, $p=0.001$. VE-VCO2 180s did not correlate with age, LVEF, CHF aetiology. VE-VCO2 180s had good reproducibility with variability coefficient=8.5% (2 CPX within 2-7 days, in 14 patients). During the follow-up (mean: 669 ± 396 days) 40 (20%) patients died. Elevated VE-VCO2 180s ($>$ mean+2SD of age-matched controls, ie VE-VCO2 180s >32.5) was related to impaired survival in univariate analysis (hazard ratio 2.8, 95%CI: 1.5-5.5, $p=0.002$). Multivariate analysis identified only VE-VCO2 180s ($p<0.05$), but not NYHA class ($p=0.1$) and peakVO2 ($p=0.2$) as conveying significant independent prognostic information.

Conclusions. In pts with CHF an excessive ventilation to early phase of exercise carries an important clinical and prognostic information. Our findings extend the application of the ventilatory assessment for prognostic stratification to CHF pts who are not able to perform maximal CPX.

1033-118 Noninvasive Assessment of Coronary Artery Flow and Reserve in Top Athletes: Relationship With Oxygen Uptake

Fausto Rigo, Carlo Zanella, Valeria Cutaia, Ugo Coli, Claudio Rigo, Antonio Raviele, Mestre-Venice, Italy

Background: Coronary flow reserve (CFR) can be measured by transthoracic echocardiography (TTE) during vasodilator stress on mid-distal left anterior descending (LAD). The Athletes (A) have higher aerobic performances (VO_2max) in comparison with sedentary subjects. The aim of our study was to verify the relationship between CFR and VO_2max in A.

Methods: Starting from January 2002, 36 consecutive elite soccer A (36 males; age= 29 ± 8 years) were evaluated by stress echocardiography. TTE (S8 probe, second harmonic 7 MHz, HP 5500, Agilent technology). Mid-distal LAD coronary artery was imaged from a modified apical two-chamber view. Wherever color-coded blood flow from the baseline could not be obtained, contrast enhancement with Levovist (Schering AG, 300 mg/ml/min) was used. Peak diastolic coronary flow velocity of each coronary artery was recorded by pulsed Doppler under the guidance of Color Doppler flow mapping. CFR was calculated as the ratio of diastolic flow velocity /rest peak diastolic flow velocity (0.84 mg over 6 m).

Results: Interpretable rest-peak signals were obtained in all 36 A for LAD (100%). The CFR mean value on LAD was 4.5 ± 5 (range: $2.8-5.9$); the mean value of VO_2max was 40 ± 6 ml/kg/min (range: $36-45$ ml/kg/min). CFR and VO_2max were significantly correlated ($r=0.73$; $p<0.0001$).

Conclusion: With latest generation, high frequency, second harmonic, contrast-enhanced transthoracic echocardiography, imaging of LAD coronary artery flow and assessment of flow reserve is highly feasible in A. This noninvasive parameter shows a strict relationship with the aerobic performances in A, confirming that the VO_2max represents a powerful metabolic trigger of CFR. Combined assessment of CFR and VO_2max allows a more complete functional evaluation of "the athlete's heart".

POSTER SESSION

1049 Natriuretic Peptides

Sunday, March 07, 2004, 3:00 p.m.-5:00 p.m.

Morial Convention Center, Hall G

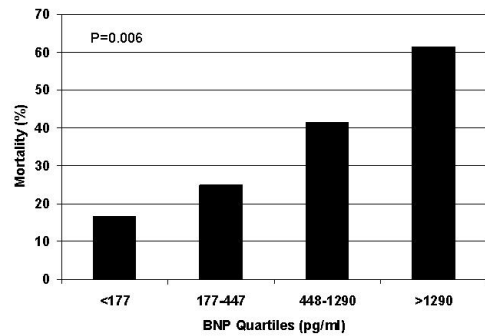
Presentation Hour: 4:00 p.m.-5:00 p.m.

1049-103 B-Type Natriuretic Peptide Strongly Predicts Mortality in Intensive Care Unit Shock

Roderick H. Tung, Christine Garcia, Richard Pino, Alexander M. Morss, Kent Lewandrowski, Elizabeth Lewandrowski, B. Taylor Thompson, Michael A. Fifer, James L. Januzzi, Jr., Massachusetts General Hospital, Boston, MA

Background. B-type natriuretic peptide (BNP) levels predict mortality across a wide range of cardiovascular syndromes. The prognostic utility of BNP in the intensive care unit (ICU) setting has not been evaluated. **Methods.** 49 consecutive patients with shock of various etiologies were enrolled. Analysis for BNP and calculation of APACHE II scores were performed at the time of enrollment. Log-transformed BNP values were divided into quartiles and correlated with in-hospital mortality. Logistic regression analysis identified independent predictors of ICU death. **Results.** A wide range of BNP levels was observed (<5 to >5000 pg/ml), with a mean BNP of 1133 ± 1416 pg/ml. 18 patients (37%) died during the course of the study. Mean (\pm SD) BNP levels were significantly higher in patients dying than in survivors (1891 ± 1853 vs 653 ± 754 pg/ml, $p=0.002$). Across log quartiles of BNP, there was significant correlation between logBNP levels and mortality risk (Figure, $p=0.006$). Among the 13 patients in the highest log quartile (BNP >1290 pg/ml) the risk of mortality was 62%. Notably, only one of these patients had cardiogenic shock. Logistic regression analysis identified a logBNP level in the highest quartile as a significant predictor of mortality ($p=0.001$). In contrast, the value of APACHE II scores for predicting mortality was less evident.

Conclusion. Among ICU patients with shock of various etiologies, BNP levels powerfully predicted mortality, and were superior to APACHE II scores for this purpose.



1049-104

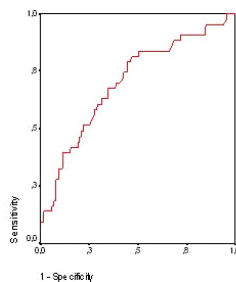
Correlation Between Brain Natriuretic Peptide and Cardiopulmonary Exercise Test Parameters in Patients With Chronic Heart Failure

Angela Beatrice Scardovi, Nadia Aspromonte, Claudio Coletta, Elena Cerquetani, Mauro Romano, Tiziana Di Giacomo, Manuela Greggi, Vincenzo Ceci, S. Spirito Hospital, Rome, Italy

We sought to evaluate if brain natriuretic peptide (BNP) levels are associated with exercise capacity determined by cardiopulmonary exercise test (CPx) in patients (pts) suffering from CHF. One-hundred sixty-five consecutive pts with CHF (age 70; beta blockers 53%; ischemic CHF: 52%; mean ejection fraction 41%; NYHA class I: 8%; II: 68%; III: 24%) were considered. Mean BNP was 228 ± 277 pg/ml (Biosite Diagnostic, Triage BNP Test). CPx parameters were: $\dot{V}O_2$ peak ($\dot{P}VO_2$) (12.35 ± 4.48 ml/Kg/min), anaerobic threshold (AT) (9.43 ± 2.80 ml/Kg/min), ventilation and carbon dioxide production ratio ($\dot{V}E/\dot{V}CO_2$) (38.02 ± 8.27), $\dot{V}E/\dot{V}CO_2$ slope (33.82 ± 7.78).

Results: A reverse statistically significant correlation between BNP level, $\dot{P}VO_2$ ($r = -0.297$; $p < 0.0001$) and AT ($r = -0.271$; $p < 0.05$) was respectively observed. A significant correlation between BNP and abnormally high ventilatory response to exercise, expressed as $\dot{V}E/\dot{V}CO_2$ ($r = 0.345$; $p < 0.0001$) and $\dot{V}E/\dot{V}CO_2$ slope ($r = 0.432$; $p < 0.0001$) was observed. The ROC curves demonstrated BNP ≥ 97 pg/ml to be the best cut-off for determining $\dot{P}VO_2 < 14$ ml/Kg/min, with overall accuracy of 71% (sensitivity: 65%; specificity: 65%), area under the curve (AUC): 0.69. Moreover, ROC demonstrated BNP ≥ 138 pg/ml to be the best cut-off for determining $\dot{P}VO_2 < 10$ ml/Kg/min, with overall accuracy 62% (sensitivity: 67%; specificity: 64%), AUC 0.72. BNP offers an alternative tool for distinguishing pts with moderate-to-severe reduction of exercise capacity.

ROC

BNP vs $\dot{P}VO_2 < 10$ ml/Kg/min

AUROC: 0.702 (95% CI: 0.60 to 0.79)

1049-105

Increased Plasma Levels of Nt-ProANP and Nt-ProBrain Natriuretic Peptide as Markers of Cardiac Depression in Septic Patients

Ursula Hoffmann, Martina Brueckmann, Thomas Bertsch, Claudia Liebetrau, Martin Borggreffe, Guenter Huhle, Karl K. Haase, University Clinic Mannheim, Mannheim, Germany

Background: The family of natriuretic peptides comprises several structurally-related 22-53-amino acid peptides, such as atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP), which are vasoactive peptides that have vasodilator and diuretic properties and play an important role in cardiovascular homeostasis. The salutary cardiovascular effects of natriuretic peptides suggest that ANP and BNP have a pathophysiological significance in cardiac depression in septic patients. Aim of the present study was to determine plasma levels of the stable N-terminal prohormone forms of ANP (Nt-proANP) and BNP (Nt-proBNP) in septic patients and healthy controls.

Patients and Methods: Nt-proANP and Nt-proBNP levels were measured in plasma samples from 18 septic patients at day 1 of severe sepsis and 13 healthy controls by ELISA- methods.

Results: The mean APACHE-Score of septic patients was $16.8 \pm SD = 4.0$ on day 1. Ten of the 18 septic patients died (55% = non-survivors). Significantly higher concentrations ($p = 0.006$) of Nt-proANP were measured in non-survivors ($MW = 13415$ fmol/l \pm SEM = 3640) as compared to controls ($MW = 2274$ fmol/ml \pm SEM = 1043). There was also a significant difference between Nt-proANP levels in controls and survivors ($p = 0.019$). There were no differences of Nt-proANP levels between survivors and non-survivors ($p = 0.189$). Levels of Nt-proBNP were also significantly higher in non-survivors ($MW = 3439$ fmol/l \pm SEM = 1246; $p = 0.010$) and survivors ($MW = 1009$ fmol/l \pm SEM = 263; $p = 0.001$) as compared to controls ($MW = 200$ fmol/l \pm SEM = 24). There was no significant difference between concentrations of Nt-proBNP in the non-survivor and the survivor-group.

Conclusion: Nt-proANP and Nt-proBNP levels are elevated in the early course of septic patients, possibly reflecting myocardial depression in severe sepsis.

1049-106

Endothelial Marker Big Endothelin-1 Is More Discriminant Than Brain Natriuretic Peptide to Categorize Patients With Congestive Heart Failure

Ronald Van Beneden, Michel P. Hermans, Sylvie A. Ahn, Jean-Marie Ketelslegers, Michel F. Rousseau, University of Louvain, Brussels, Belgium

Background: Brain Natriuretic Peptide (BNP) and Big Endothelin-1 (BigET-1) are becoming central as diagnostic and prognostic neurohormonal markers to the management of patients with congestive heart failure.

Methods: The Discriminant Ratio (DR) method (Levy JC et al. Am J Physiol 276: E365-E375, 1999) was used to compare the respective performance of BNP and BigET-1 to rank patients according to heart failure severity. The DR estimates the ability of a method to discriminate subjects. It is obtained from the ratio of the underlying between-subject standard deviation (SDu) to the within-subject SD (SDw). DRs were calculated from BNP and BigET-1 duplicates, sampled on 2 consecutive days. Significance of differences in DRs was $p < 0.05$. Correlation coefficients between pairs of measurements were adjusted in order to include an estimate of the underlying correlation, since standard coefficients, due to the presence of within-subject variation, tend to underestimate the true correlation between tests through attenuation. An unbiased estimation of the linear relationship equation between methods was also derived.

Results: Plasma concentrations of BNP and BigET-1 were measured in duplicates in 31 heart failure patients (NYHA II-IV, mean EF 23%). Mean values of day 1 and day 2 (\pm SD) were 75 (52) and 77 (52) pg/mL for BNP [normal values (range): 5.4 (2.5-12.8) pg/mL], and 12.5 (7.4) and 12.0 (8.1) pg/mL for BigET-1 [normal values (range): 5.7 (4.0-7.6) pg/mL], respectively. The difference between the DRs of BNP and BigET-1 (2.73 and 4.61 respectively) was statistically significant ($p < 0.05$) in favor of a better discriminating ability for BigET-1. Unadjusted Pearson coefficient between methods was 0.70, rising up to 0.83 following adjustment for attenuation. Slope and intercept of the unbiased estimation of the linear relationship equation between measurements were 0.18 and -1.47 pg/mL, respectively.

Conclusions: According to the DR method, BigET-1 appears able to better discriminate a heart failure population than BNP. Although both markers are highly correlated in this population, BigET-1 is the choice method to categorize patients with congestive heart failure.

1049-107

Natriuretic Peptides as Predictors of Clinical Course in Patients With End-Stage Heart Failure

Evgenij V. Potapov, Frank D. Wagner, Felix Hennig, Christian Müller, Rainer Michael, Hans B. Lehmkuhl, Roland Hetzer, Deutsches Herzzentrum Berlin, Berlin, Germany, Charité, Humboldt University, Germany

Background: The optimal timing for heart transplantation (HTx) or implantation of a ventricular assist device (VAD) in patients with end-stage heart failure is a key issue.

Methods: In 86 patients with end stage heart failure requiring inotropic support and scheduled for HTx or VAD implantation blood was sampled daily. Big endothelin-1 (big ET-1) and natriuretic peptides (pro-ANP, ANP, NT-proBNP and BNP) were measured at the end of the study. Clinical and hemodynamic parameters were also evaluated daily.

The patients were divided into groups with regard to the following endpoints: Group I – immediate VAD placement due to profound cardiogenic shock on admission ($n = 10$); Group II – deterioration into cardiogenic shock after an initially stable clinical course ($n = 26$); Group III – stable clinical course allowed urgent HTx or VAD implantation ($n = 41$); Group IV – weaning from inotropic support ($n = 9$). The data are presented as median values.

Results: On admission there were no differences in clinical parameters between the